#### VPI/99-06 CON

# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner

: Not Yet Assigned

Group Art Unit

Not Yet Assigned

**Applicants** 

Francis Salituro et al.,

Serial No.

Not Yet Assigned

Filed

Herewith

:

For

INHIBITORS OF C-JUN N-TERMINAL KINASES

(JNK)

Cambridge, Massachusetts November 30, 2001

Hon. Assistant Commissioner For Patents Washington, D.C. 20231

# PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115(a)

Sir:

Preliminary to examination of the above-identified application, kindly amend the application as follows:

## **IN THE SPECIFICATION**

On page 1, immediately after the title, insert

### ■ CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuing application of co-pending International Patent Application PCT/US00/15248, filed June 2, 2000, which claims priority of United States provisional patent application 60/137,523, filed June 3, 1999. --

#### **REMARKS**

In former specification page 1, after the title of the specification and before the section entitled "TECHNICAL FIELD OF THE INVENTION", applicants have inserted a paragraph, entitled "CROSS-REFERENCE TO RELATED APPLICATIONS", which properly sets forth the claims to priority.

Pursuant to 37 C.F.R. § 1.121(b)(1)(iii), the above amendments are set forth in the enclosed marked up copy of substitute specification page 1 (see, Appendix A). Applicants have also enclosed, pursuant to 37 C.F.R. § 1.121(b)(1)(ii), a clean form of substitute specification page 1, incorporating the above amendments (see, Appendix B).

None of the above amendments adds any new matter.

#### **CONCLUSION**

Applicants request that the Examiner enter the above amendments, and allow the pending claims to pass to issue.

Respectfully submitted,

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This application is a continuation of co-pending International Application PCT/US00/15248, filed June 2, 2000, which claims priority of United States provisional patent application 60/237,523, filed June 3, 1999.

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INHIBITORS OF C-JUN N-TERMINAL KINASES (JNK)

### TECHNICAL FIELD OF INVENTION

The present invention relates to inhibitors of c-Jun N-terminal kinases (JNK), which are members of the mitogen-activated protein (MAP) kinase family. There are a number of different genes and isoforms which encode JNKs. Members of the JNK family regulate signal transduction in response to environmental stress and proinflammatory cytokines and have been implicated to have a role in mediating a number of different disorders. The invention also relates to methods for producing these inhibitors. The invention also provides pharmaceutical compositions comprising the inhibitors of the invention and methods of utilizing those compositions in the treatment and prevention of various disorders.

### BACKGROUND OF THE INVENTION

Mammalian cells respond to extracellular stimuli

20 by activating signaling cascades that are mediated by
members of the mitogen-activated protein (MAP) kinase
family, which include the extracellular signal regulated
kinases (ERKs), the p38 MAP kinases and the c-Jun Nterminal kinases (JNKs). MAP kinases (MAPKs) are

25 activated by a variety of signals including growth
factors, cytokines, UV radiation, and stress-inducing
agents. MAPKs are serine/threonine kinases and their
activation occur by dual phosphorylation of threonine and